esters; ii) with polyalcohols of the aliphatic, aromatic, arylaliphatic, cycloaliphatic, heterocyclic series, generating crosslinking by means of spacer chains.

The above said sulphated compounds obtained according to the process of the present invention can be optionally salified with heavy metals, the heavy, metals being selected from the group of metal elements in the 4th, 5th and 6th periods of the periodic table, such as silver, iron, cobalt, copper, zinc, arsenic, strontium, zirconium, antimony, gold, cesium, tungsten, selenium, platinum, ruthenium, bismuth, tin, titanium and mercury.

D1 (cancel)

REMARKS

This Amendment is being filed in response to the Office Action that was mailed May 20, 2002.

A copy of page 1070 of the Sigma catalog is attached to this paper.

The amendment to the specification that was set forth in the Amendment that was dated September 4, 2001 is being resubmitted with the correction that was made in the Amendment dated January 22, 2002 and the full text of the amendatory language to the specification that was submitted in the Amendment dated September 4, 2001.

An early and favorable action is earnestly solicited.

Respectfully Submitted

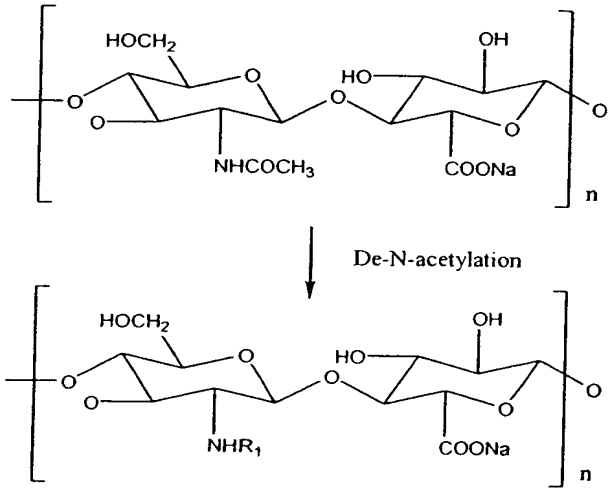
James V. Costigan
Registration No. 25,669

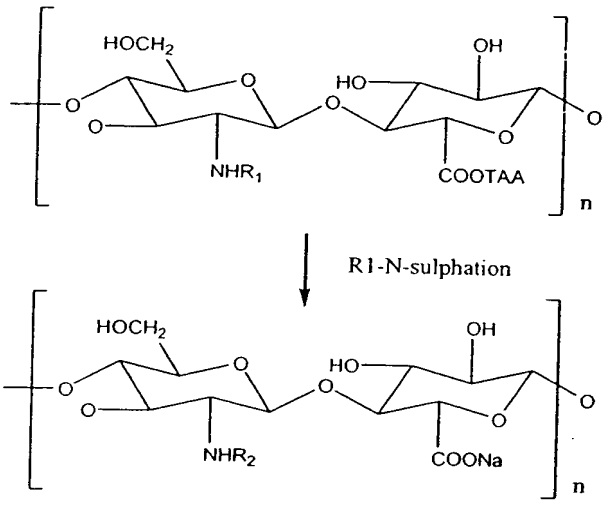
HEDMAN & COSTIGAN, P.C.
1185 Avenue of the Americas
New York, NY 10036
(212) 302-8989

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on 6/19/02

Marked up copy of amendments to specification:

By sulphated hyaluronic acid and sulphated hyaluronic acid derivatives, we mean:
A_1) O-sulphated hyaluronic acid, and
A_2) O-sulphated hyaluronic acid derivatives,
both types being disclosed in U.S.Patent No. 6,051,701, which is incorporated herewith by reference;
B_1) N-sulphated hyaluronic acids, and
B_2) N-sulphated hyaluronic acid derivatives,
both types being obtainable by means of a controlled sulphation reaction on the amino group of glucosamine of hyaluronic acid, previously deacetylated according to the procedure described by P. Shaklee (1984) Biochem. J., 217, 187-197. The reaction proceeds as illustrated below:





n: from 12 to 12,500

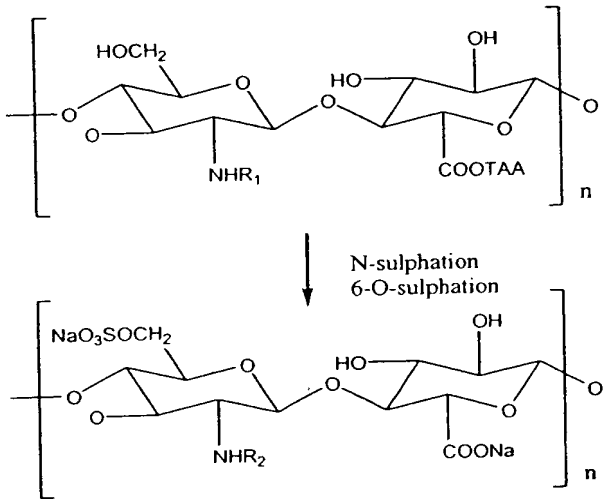
R_1 = H, $COCH_3$

TAA = tetra-alkylammonium

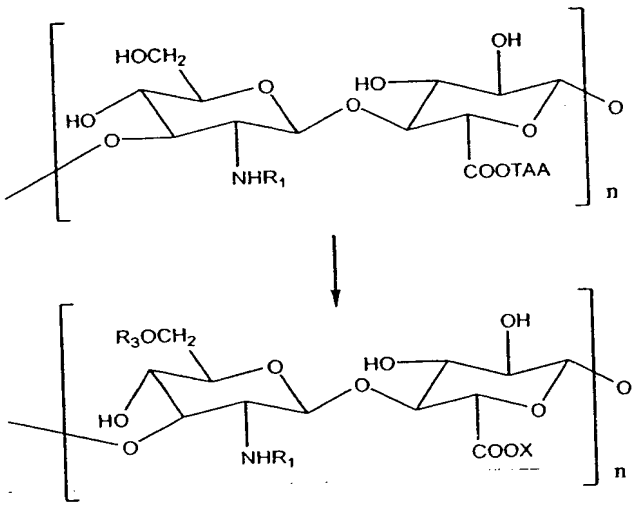
R_2 = SO_3, $COCH_3$

Diagram 1

b) and c) mean the products of the chemical reaction illustrated in Diagram 1, wherein, besides the amino group of glucosamine, the primary hydroxy function of the same residue is also totally or partially involved in the sulphation reaction, as illustrated below:



The derivatives generated according to diagrams 1 and 2 can be used as intermediate reactants in the preparation of compounds, according to the procedure described in U.S. 4,851,521, wherein the carboxy function of the glucuronic residue of hyaluronic acid, partially 2-N-sulphated or partially 2-N-sulphated and partially or totally 6-O-sulphated, is partially or completely reacted with alcohols of the aliphatic, aromatic, arylaliphatic, cycloaliphatic, heterocyclic series, producing the respective partial or total esters:



n: from 12 to 12,500

R_1 = H, $COCH_3$

TAA = tetra-alkylammonium

R_2 = SO_3, $COCH_3$

R_3 = SO_3, H

X = alcoholic residue, Sodium

Diagram 3

Moreover it is possible to use the synthetic derivatives according to diagrams 1 and 2 as intermediates in the

preparation of crosslinked compounds, according to the procedures described in U.S. 5,676,964 and U.S. 4,957,744 respectively, wherein a part or all of the carboxy groups belonging to the D-glucosamine residue are reacted: i) using condensing agents with the alcoholic functions of the same polysaccharide chain or other chains, generating inner (or lactone) esters and intermolecular esters; ii) with polyalcohols of the aliphatic, aromatic, arylaliphatic, cycloaliphatic, heterocyclic series, generating crosslinking by means of spacer chains.

The above said sulphated compounds obtained according to the process of the present invention can be optionally salified with heavy metals, the heavy, metals being selected from the group of metal elements in the 4^{th}, 5^{th} and 6^{th} periods of the periodic table, such as silver, iron, cobalt, copper, zinc, arsenic, strontium, zirconium, antimony, gold, cesium, tungsten, selenium, platinum, ruthenium, bismuth, tin, titanium and mercury.